Health Technology Briefing
September 2025

Pozelimab with cemdisiran for treating generalised myasthenia gravis

Company/Developer	Regeneron Pharmaceuticals Inc

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 34081	NICE ID: Not available	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Pozelimab with cemdisiran is currently in development for the treatment of generalised myasthenia gravis (gMG). Myasthenia gravis (MG) is a long-term condition that causes muscle weakness with the muscles around the eyes usually affected first. gMG begins in the eyes and spreads to other muscle groups in the body. This type is more common. MG is more common in women than men. Symptoms usually start in women under 40 years and men over 60 years, but the condition can affect people of all ages. Current treatment aims to keep the symptoms of MG under control so that the patient can live as close to a normal life as possible. However, these treatments often cause long-term side effects that can be intolerable for patients, and some individuals become refractory.

Pozelimab and cemdisiran are both injected into the fat under the skin. Pozelimab is a type of protein that recognises another specific protein in the body called C5. Pozelimab attaches to C5, thereby helps stops the immune system from attacking the body and causing inflammation. Cemdisiran works by stoppings the liver from making C5. By lowering C5, both drugs help protect muscle damage. This helps to improve muscle strength and reduce symptoms in patients with gMG. If approved, pozelimab and cemdisiran will provide a new treatment option for patients with gMG.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Proposed Indication

Treatment of symptomatic generalised myasthenia gravis (gMG).[1]

Technology

Description

Pozelimab (REGN3918) is a human immunoglobulin G4 monoclonal antibody (mAb) directed against terminal complement protein C5, with potential anti-inflammatory activity.[1,2] Upon administration, pozelimab targets and binds to terminal complement protein C5, thereby blocking C5 cleavage into pro-inflammatory components and preventing the complement-mediated destruction of red blood cells. C5, a complement pathway protein, is expressed at high levels by the liver.[2]

Cemdisiran (ALN-CC5) is composed of small-interfering RNAs (siRNAs) directed against terminal complement component 5 of the complement pathway conjugated to a N-acetylgalactosamine (GalNAc) ligand.[1,3] Upon administration of cemdisiran, the GalNAc ligand moiety specifically binds to and is taken up by the asialoglycoprotein receptor (ASGPR) expressed on liver cells. Inside the cell, the siRNAs bind to C5 mRNAs, which results in the inhibition of both the translation and expression of the C5 protein. This lowers plasma C5 levels, prevents C5 cleavage into pro-inflammatory components and blocks complement-mediated haemolysis.[3]

Pozelimab in combination with cemdisiran is currently in clinical development for the treatment of gMG. In the phase III clinical trial (NIMBLE, NCT05070858), participants are given pozelimab and cemdisiran via subcutaneous (SC) administration.[1]

Key Innovation

About 10–20% of myasthenia gravis (MG) patients do not achieve an adequate response or are intolerant to conventional treatment.[4] Conventional treatments such as corticosteroids and other immunosuppressive agents come with a wide range of often debilitating side effects. Thus, demonstrating an urgent need for targeted treatments with sustained efficacy and improved safety to adequately manage MG symptoms and reduce MG related disease burden.[5,6] The increasing understanding of the biologic pathogenic pathways of MG has allowed in the latest years to conceive new drugs with a more targeted effect. In particular, the last decade has seen a wide range of mAbs being applied in MG with promising results.[6] Complement component C5 is a clinically validated target for gMG.[7] Targeted immunotherapy seems to be the most promising therapeutic approach in MG because it can effectively overcome the limitations of current nonspecific immunotherapies and has the potential to induce remission.[8]

Pozelimab is a human mAb against C5 complement whereas cemdisiran is a siRNA which can suppress the hepatic production of C5. Both drugs are generally safe and well-tolerated at different doses.[9] The combination of pozelimab and cemdisiran has previously mediated complement activity inhibition more efficiently than either pozelimab or cemdisiran administered alone.[7] Moreover, both drugs are SC administered, which enhances patient convenience and adherence.[10,11] If licensed, pozelimab in combination with cemdisiran will offer an additional treatment option for patients with symptomatic gMG.

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Regulatory & Development Status

Pozelimab does not currently have Marketing Authorisation in the EU/UK for any indication.

Cemdisiran does not currently have Marketing Authorisation in the EU/UK for any indication.

Pozelimab as monotherapy is in phase III/II clinical development for CD55-deficient protein-losing enteropathy.[12]

Pozelimab in combination with cemdisiran is also in phase III/II clinical development for:[12,13]

- Paroxysmal nocturnal hemoglobinuria
- Age-related macular degeneration (specifically geographic atrophy)

Patient Group

Disease Area and Clinical Need

MG is a rare chronic autoimmune condition that causes fatigable muscle weakness.[14] It most commonly affects the muscles that control the eyes and eyelids, facial expressions, chewing, swallowing and speaking. However, it can affect most parts of the body.[15] In MG, certain antibodies mistakenly interfere with the signals that travel between the nerves and muscles. The complement system normally helps to protect against certain types of infections. But in MG, the complement system attacks and destroys the neuromuscular junction—the area where the nerves and muscles meet. The resulting damage can cause muscle weakness, which may contribute to MG symptoms.[16] gMG begins in the eyes and spreads to other muscle groups in the body. This type is more common.[14] Common symptoms of MG include droopy eyelids, double vision, difficulty making facial expressions, problems with chewing and swallowing. Other symptoms include slurred speech, weak arms, legs or neck, shortness of breath, and occasionally serious breathing difficulties.[15] In addition, in about 10% of affected individuals may develop potentially life-threatening complications due to severe involvement of muscles used during breathing (myasthenic crisis).[17] Refractory MG affects about 1 in 5 people, who will experience persistent or worsening symptoms despite medication, and treatment options are limited.[14]

The prevalence of MG in the UK is estimated at about 33.7 per 100,000 persons in the UK.[18] It can affect people of any age, typically starting in women under 40 years and men over 60 years.[15] In England, 2023-24, there were 5,941 finished consultant episodes (FCE) and 4,384 FCE admissions for MG (ICD-10 code G70.0) which resulted in 16,931 FCE bed days and 2,957 day cases.[19]

Recommended Treatment Options

There is currently no treatment option recommended by the National Institute for Health and Care Excellence (NICE) for MG.

The British National Formulary (BNF) recommends the following pharmacological treatment options to treat gMG:[20]

- Anticholinesterases such as neostigmine and pyridostigmine bromide are used as an adjunct to immunosuppressant therapy for gMG.
- Corticosteroids such as prednisolone is used when anticholinesterases do not control symptoms completely. A second-line immunosuppressant such as azathioprine is frequently used to reduce the dose of corticosteroid.

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- Plasmapheresis or infusion of intravenous immunoglobulin [unlicensed indication], may induce temporary remission in severe relapses, particularly where bulbar or respiratory function is compromised or before thymectomy.

Clinical Trial Information

Trial	**NIMBLE,** NCT05070858, EudraCT 2020-003272-41, CTIS 2023-508842-17-00; Efficacy and Safety of Pozelimab and Cemdisiran Combination Therapy and Cemdisiran Monotherapy in Patients With Symptomatic Generalized Myasthenia Gravis **Phase III** - Recruiting **Location(s):** Eight EU countries, UK, USA, Canada and other countries **Primary completion date:** July 2025 (Estimated)
Trial Design	Randomised, parallel assignment, quadruple-blinded
Population	N = 335 (estimated); subjects with symptomatic gMG; aged 18 years and over.
Intervention(s)	Pozelimab SC and cemdisiran SC combination therapy
Comparator(s)	Matched placebo
Outcome(s)	Change in MG-ADL total score [Time Frame: From baseline to week 24]. The total MG-ADL score ranges from 0 to 24 points, with higher scores indicating greater functional impairment and disability.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of pozelimab is not yet known.

The cost of cemdisiran is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal awaiting development. Inebilizumab for treating generalised myasthenia gravis [ID6587] [TSID12110] (GID-TA11667). Expected date of issue to be confirmed.
- NICE technology appraisal awaiting development. Nipocalimab for treating generalised myasthenia gravis [ID6562] (GID-TA11492). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Zilucoplan for treating antibody positive generalised myasthenia gravis [ID4008] (GID-TA11096). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Rozanolixizumab for treating antibody-positive generalised myasthenia gravis [ID5092] (GID-TA10994). Expected date of issue to be confirmed.
- NICE guideline. Suspected neurological conditions: recognition and referral (NG127). May 2019.

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NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: Rituximab bio-similar for the treatment of myasthenia gravis (adults). 170084P. September 2018.
- NHS England. 2014/15 NHS Standard Contract for Neuromuscular Operational Delivery Network Specification. D04/ODN/a.
- NHS England. 2013/14 NHS Standard Contract for Neurosciences: Specialised Neurology (Adult). D04/S/a.
- NHS England. 2013/14 NHS Standard Contract for Diagnostic Service for Rare Neuromuscular Disorders (All ages). D04/S(HSS)/a.

Other Guidance

- Myasthenia Gravis Foundation of America (MGFA). International Consensus Guidance for Management of Myasthenia Gravis: 2020 Update. 2021.[21]
- MGFA. International Consensus Guidance for Management of Myasthenia Gravis: Executive summary. 2016.[22]
- Association of British Neurologists. Myasthenia gravis: Association of British Neurologists' management guidelines. 2015.[23]

Additional Information

Regeneron Pharmaceuticals Inc did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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